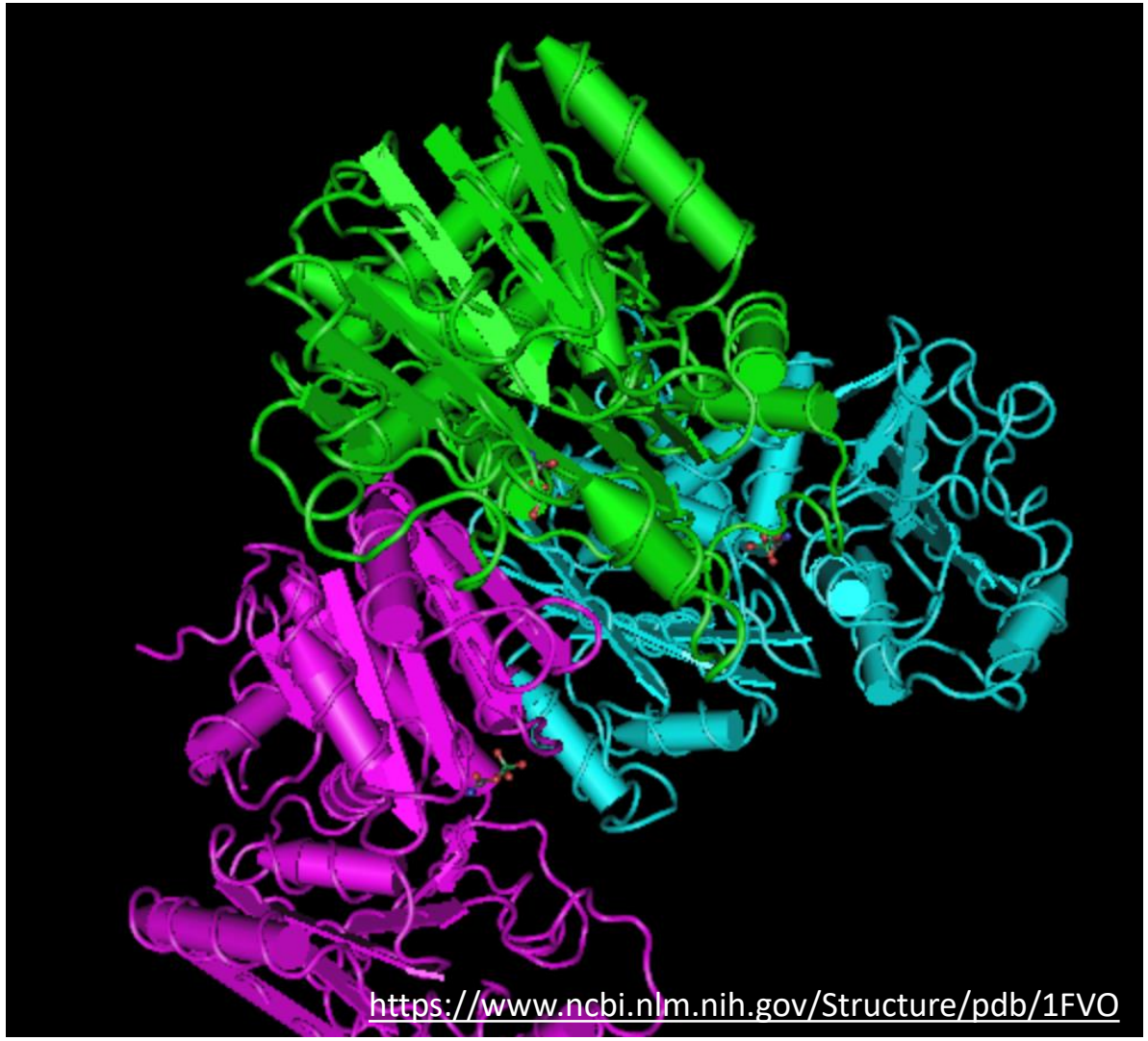
Ornithine transcarbamylase deficiency



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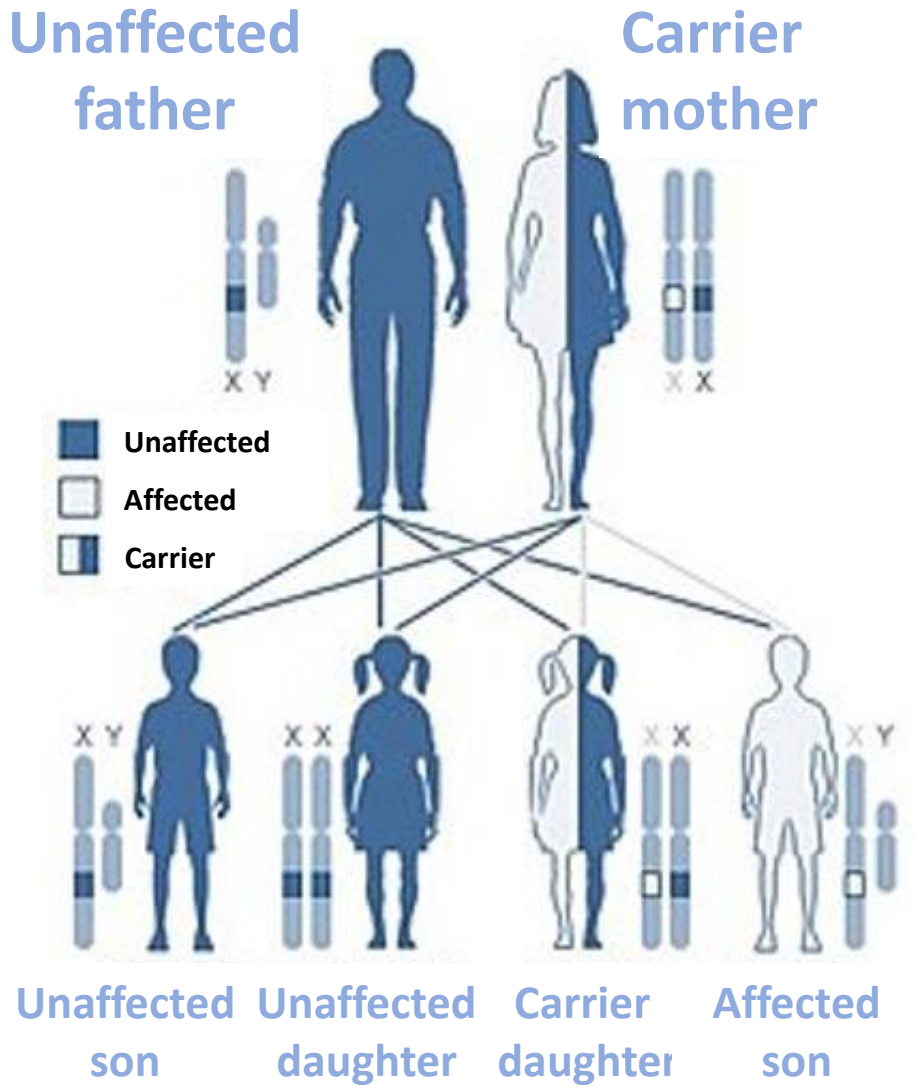
History, Occurrence, and Provenance

- Ornithine Transcarbamylase Deficiency (OTCD) is caused by a mutation in the gene encoding ornithine transcarbamylase enzyme
- Originally documented in 1962 in two female cousins, who failed to thrive and had increased ammonia levels in the blood
- Estimated to be present at a frequency of 1/14,000 to 1/77,000
- More common and severe in males
- Typically diagnosed in newborns but can present at any time in life

Genetics: OTCD is a X-linked, recessive disease

- It is unlikely for a female to have two mutated X chromosomes, so females usually still have a source for functional protein and have less severe symptoms
- If males have their X chromosome mutated, they have no way of making up for the deficiency and their symptoms are usually much more severe than for females



Digital image retrieved Oct. 23, 2018 from https://ghr.nlm.nih.gov/

X-linked Inheritance

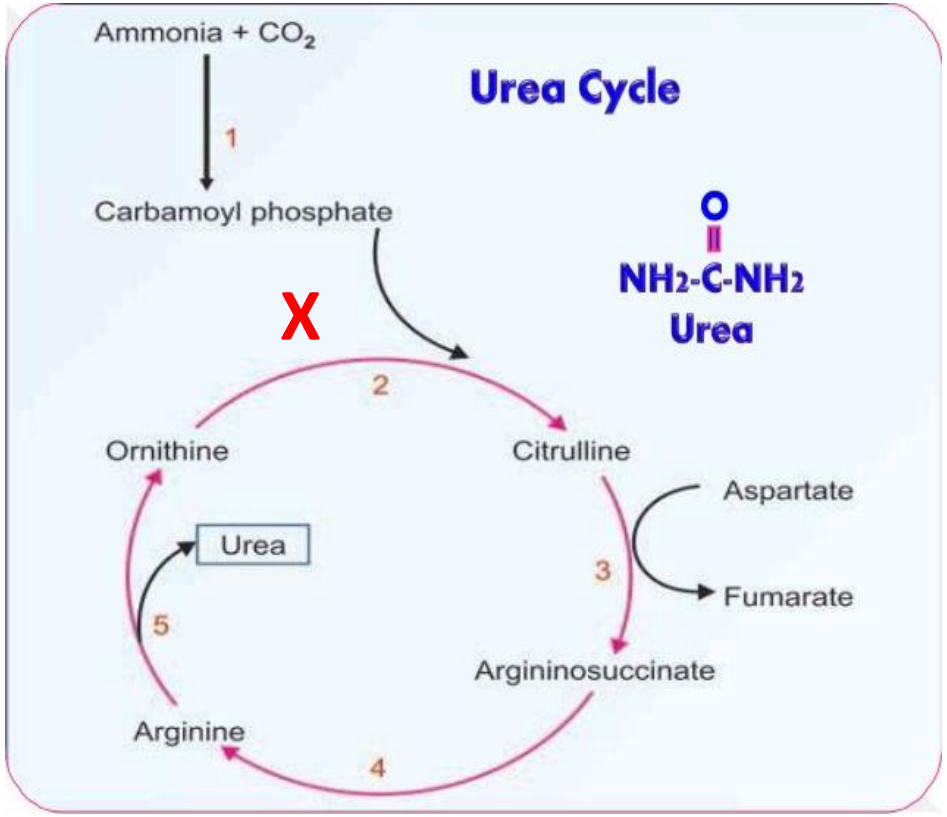
Medicine, UCD, director. *X Linked Recessive*. *YouTube*, YouTube, 1 Sept. 2014, www.youtube.com/watch?v=Vdam8pKhRNo.

Biochemical Features

- Converting ammonia to urea requires five different enzymes, which assist chemical reactions in the body

- One of these enzymes is ornithine transcarbamylase

- A deficiency in ornithine transcarbamylase is a roadblock in the urea cycle and causes a buildup of ammonia

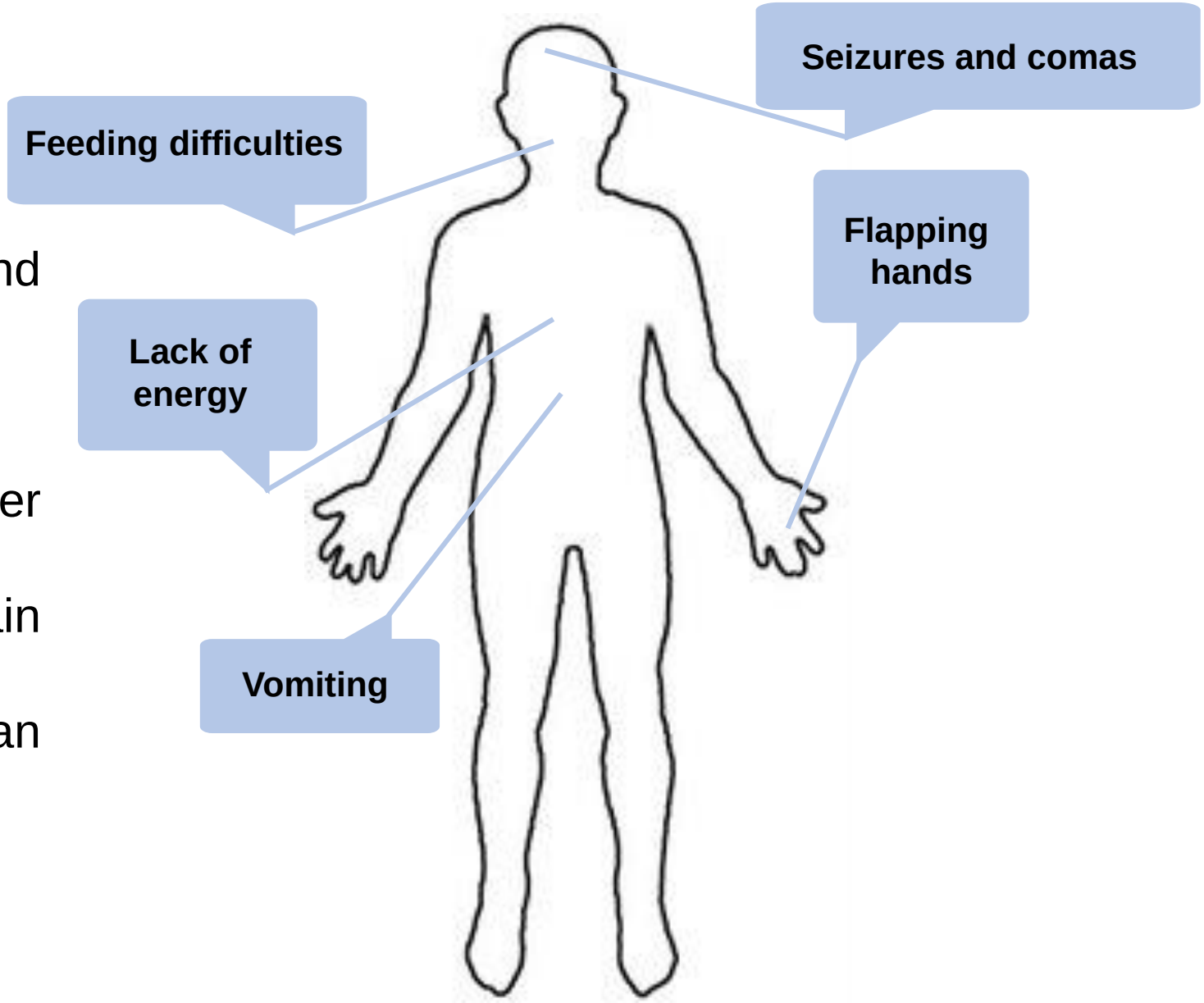


Digital image retrieved Oct. 23, 2018 from www.slideshare.net/YESANNA/urea-cycle-44200147

Symptoms

Other symptoms include:

- Difficulty breathing, sweating, and convulsions
- High levels of ammonia cause liver malfunction, leading to brain damage during what is called an encephalopathic episode



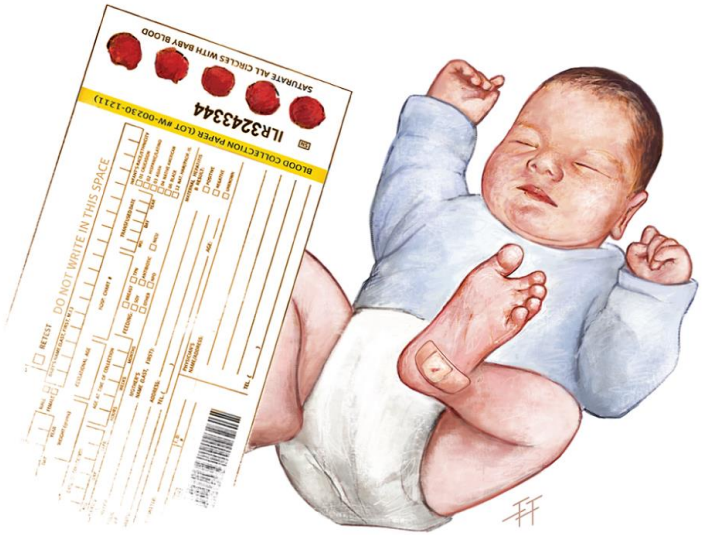
Diagnosis

Newborn screening

Identifying a buildup of ammonia

and carbamoyl phosphate as well as

a depletion of arginine and citrulline



Digital image retrieved Oct. 23, 2018 from
jamanetwork.com/journals/jamapediatrics/fullarticle/2525944

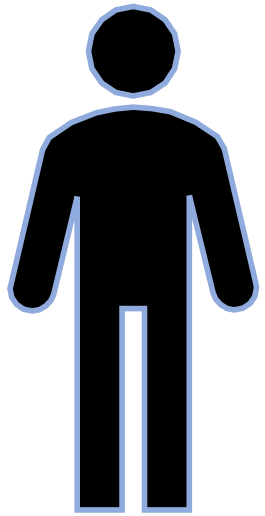
Newborn Screening. Digital image retrieved Oct. 23, 2018 from
www.genome.gov/27556918/newborn-screening-fact-sheet/

Secondary

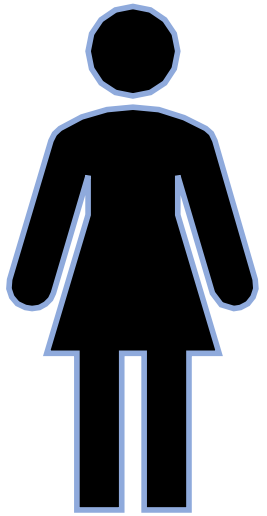
DNA sequencing to find the

OTCD-associated mutation

Prognosis



- Dietary restriction of protein
- May experience cognitive impairment
- Encephalopathic episodes can lead to coma and brain damage
- Late onset males have less severe symptoms and a longer life expectancy than males diagnosed at birth

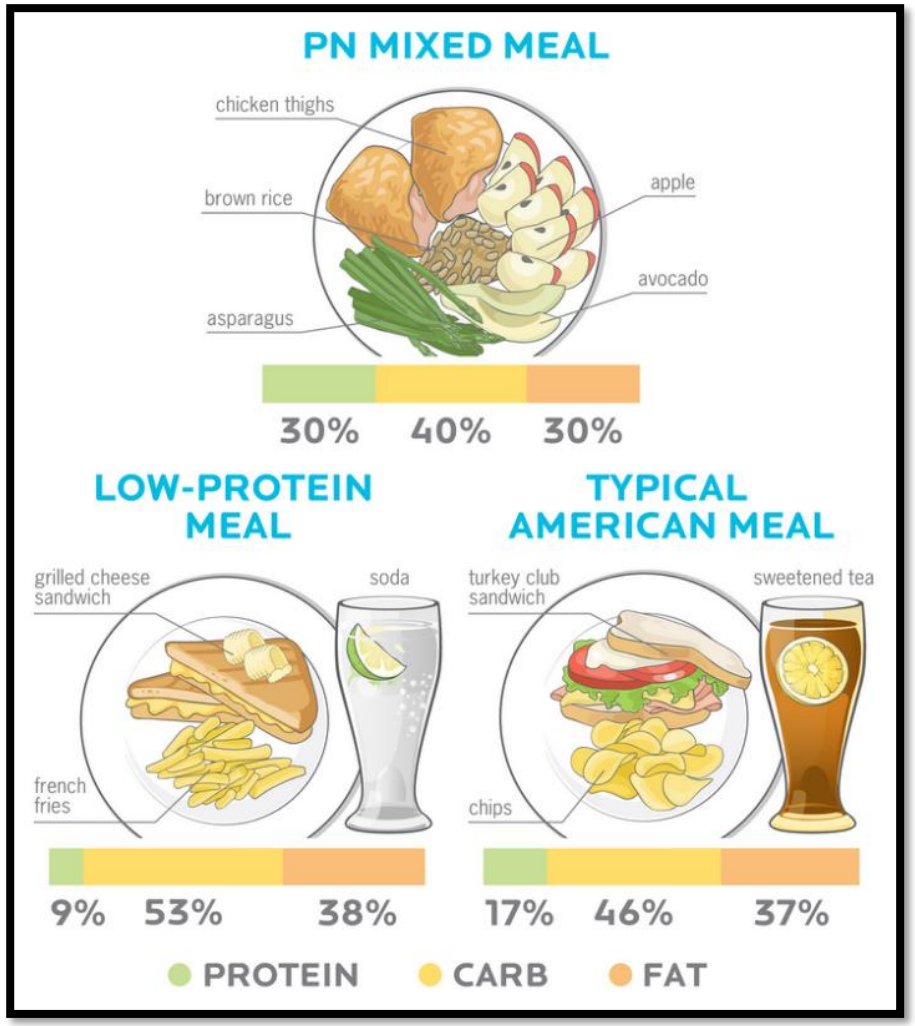


- Dietary restriction of protein
- May experience cognitive impairment
- Encephalopathic episodes can lead to coma and brain damage
- Higher chance of survival compared to males
- Varying quality of life based on level of enzyme activity

Therapy

- Low protein diet together with dietetic support as nutrition requirements change throughout human growth and development
- Supplemental arginine, sodium benzoate, and phenylbutyrate to help remove excess nitrogen from the body
- Liver transplantation, if necessary

Protein content in three types of meals



Protein Content In Three Types of Meals. Digital image retrieved Oct. 23, 2018 from www.precisionnutrition.com/will-a-high-protein-diet-harm-your-health

Read Brooke's Story

Sodium Benzoate – Possible Medication

Low-Protein Diet: Tips and Tricks

Children with Metabolic Disease Support Group

National Urea Cycle Disorders Foundation

About Newborn Screening

More Information About the Urea Cycle

*Click on the links!

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